IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Johan Weigelt et al. Art Unit : 1641
Serial No. : 09/986,240 Examiner : Deborah A. Davis
Filed : October 19, 2001
Title : NEW NUCLEAR MAGNETIC RESONANCE SCREENING METHOD

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REPLY BRIEF

Pursuant to 37 C.F.R. § 41.41, Appellants respond to the Examiner's Answer dated June 16, 2005 as follows.

Appellants also enclose herewith a Request for Oral Hearing and the requisite fee.

Please apply any other charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 13425-047001.

(I) Argument in Reply to Grounds of Rejection Presented in Examiner's Answer

Appellants rely on the Arguments set forth in the Appeal Brief and add the following comments with respect to the "Grounds of Rejection" presented at pages 3-9 of the Examiner's Answer.

As detailed in the Appeal Brief, Yabuki et al. (1998) J. BIOMOLECULAR NMR, 11:295-306 (hereinafter "Yabuki") describes a dual amino acid-selective labeling method to investigate the nature of the interaction between two proteins (Ras and Raf) that were previously known to bind to each other. According to Yabuki, "[t]his allowed us to investigate the structure of the effector region of the Ras protein complexed with Raf RBD" (Yabuki at page 306, left column).

CERTIFICATE OF MAILING BY FIRST CLASS MAIL

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Page 4 of the Examiner's Answer states that "Yabuki et al does not teach that the potential binder molecule has a molecular mass from 50-1000 Da." Appellants agree that the Ras-binding protein Raf does not have a molecular mass in the range of 50-1000 Da. However, the Examiner's use of the phrase "the potential binder molecule" in reference to the disclosure of Yabuki may be taken as a suggestion that Yabuki describes the screening of candidate molecules to determine whether they have the ability to bind to Ras. However, Yabuki contains no disclosure whatsoever related to screening candidate binding molecules to determine whether or not they posses the ability to bind to Ras. Instead, Yabuki is concerned with analyzing the structural nature of the interaction of Ras with its know ligand Raf.

The person of ordinary skill in the art, at the time the present application was filed, would have lacked the requisite suggestion or motivation to modify Yabuki in the manner contemplated by the Examiner. Moore, U.S. Patent No. 6,060,603 describes methods for modeling biologically active ligands and designing mimetics of such ligands. Moore does not describe any molecule having a molecular mass of from 50 to 1000 Da that has the ability to bind to Ras or any other protein described in Yabuki. Furthermore, nothing in Moore suggests modifying the protein structure analysis method of Yabuki to instead carry out a screening method that compares a first NMR spectra (of a labeled polypeptide or protein) and a second NMR spectra (of the labeled polypeptide or protein that has been contacted with a potential binder molecule having a molecular mass of from 50 to 1000 Da).

Because Yabuki is concerned with investigations of protein structure and the characterization of protein complexes, the skilled artisan would have had no reason to modify the methods of Yabuki to so as to perform a method that screens candidate compounds to evaluate their ability to bind to Ras or any other protein. Furthermore, neither Yabuki nor Moore describe a single low molecular weight compound (i.e., a compound having a molecular mass of from 50 to 1000 Da, as is required by the claims) that was known to bind to Ras that the skilled artisan might have attempted to use in the method of Yabuki in place of Raf to investigate the nature of a Ras-ligand interaction.

The Examiner's Answer repeats (at page 5) an assertion from the final Office Action that "absent evidence to the contrary, the range recited in the instant claims from 50-1000 Daltons is

viewed as mere optimization of the prior art assay." Because Yabuki does not describe a screening assay to identify potential binder molecules (but instead describes experiments that evaluate Ras binding to Raf), there would have been no basis or rationale for the skilled artisan to "optimize" the methods of Yabuki by, for example, replacing Raf (a known ligand of Ras) with an undefined low molecular weight compound having a molecular mass of from 50 to 1000 Da. Yabuki describes a dual amino acid-selective labeling method using a protein (Ras) and a known binding partner (Raf). As a result, it would certainly not be a "mere optimization" of Yabuki's method to remove Raf from the analysis and replace it with low molecular weight compounds having no known Ras-binding ability.

For these reasons as well as those provided in the Appeal Brief, Appellants respectfully submit that the rejection does not establish a *prima facie* showing of obviousness and request that the rejection of independent claim 1 and dependent claims 2-10 and 12 be withdrawn.

(II) Appellants Argued the Separate Patentability of Claim 12 in the Appeal Brief

Page 8 of the Examiner's Answer states that the patentability of dependent claim 12 "stands or falls with claim 1. Otherwise, appellant should have separately grouped this claim from claim 1."

Contrary to the foregoing assertion in the Examiner's Answer, Appellants argued the separate patentability of claim 12 in the Appeal Brief. The "Argument" section of the Appeal Brief was divided into subheadings (A), (B), and (C). Subheadings (A) and (B) reflected the two groupings of rejections made by the Examiner in the final Office Action dated May 4, 2004. However, subheading (C) argued the separate patentability of claim 12 and was entitled "Rejection of claim 12 under 35 U.S.C. § 103(a) as allegedly unpatentable over Yabuki in view of Moore."

37 C.F.R. § 41.37 states that "the failure of appellant to separately argue claims which appellant has grouped together shall constitute a waiver of any argument that the Board must consider the patentability of any grouped claim separately. Any claim argued separately should be placed under a subheading identifying the claim by number." Because Appellants argued the

patentability of claim 12 in the Appeal Brief under a separate subheading identifying the claim by number, the patentability of claim 12 does not stand or fall with that of claim 1.

As noted in the Appeal Brief, independent claim 12 requires that the method of independent claim 1 be used for screening a "compound library." Nothing in Yabuki or Moore, taken alone or in combination, suggests applying the dual amino acid-selective labeling method of Yabuki to a "compound library" to identify molecules in the library that bind to a polypeptide or protein of interest. In particular, there is no description whatsoever in Moore of any compound library that the skilled artisan would have had reason to use in a labeling method of Yabuki.

In support of the rejection of claim 12, the Examiner's Answer states (at page 9) that "Moore modifies the reference of Yabuki by teaching design mimetics wherein the method screens for agonist and antagonists of ligands using NMR screening techniques (col. 2, lines 66-67 and column 3, line 1)." Appellants have carefully reviewed the section of Moore cited in the Examiner's Answer as (together with the disclosure of Yabuki) allegedly rendering obvious the method of dependent claim 12. However, nothing in this cited passage refers to a "compound library" in general or any particular compound library that the skilled artisan would have had reason to use in a labeling method of Yabuki.

For these reasons as well as those provided in the Appeal Brief, Appellants respectfully submit that the rejection does not establish a *prima facie* showing of obviousness and request that the rejection of dependent claim 12 be withdrawn.

(III) Conclusion

For the foregoing reasons and the reasons stated in the Appeal Brief, Appellants submit that the final rejection should be reversed.

Respectfully submitted,

Date: August 16, 2005

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